FILE 'MEDLINE' ENTERED AT 11:45:46 ON 07 JUN 1999

FILE 'CAPLUS' ENTERED AT 11:45:46 ON 07 JUN 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'BIOSIS' ENTERED AT 11:45:46 ON 07 JUN 1999

FILE 'EMBASE' ENTERED AT 11:45:46 ON 07 JUN 1999

FILE 'WPIDS' ENTERED AT 11:45:46 ON 07 JUN 1999

Ricciglians

873601

COPYRIGHT (C) 1999 DERWENT INFORMATION LTD

L1 19 FILE MEDLINE
L2 21 FILE CAPLUS
L3 13 FILE BIOSIS
L4 18 FILE EMBASE
L5 2 FILE WPIDS

TOTAL FOR ALL FILES
L6 73 CELL AND SCAFFOLD AND (LINEAR OR FUSION PARTNER OR TARGET? SEQUE
NCE OR ADENOVIRUS)

=> s l6 and (dna or rna) and (polymerase or transcript? or nls or golgi or mitochrondria?)

L7 2 FILE MEDLINE
L8 3 FILE CAPLUS
L9 1 FILE BIOSIS
L10 1 FILE EMBASE
L11 0 FILE WPIDS

TOTAL FOR ALL FILES
L12 7 L6 AND (DNA OR RNA) AND (POLYMERASE OR TRANSCRIPT? OR NLS OR GOLGI OR MITOCHRONDRIA?)

=> dup rem l12

PROCESSING COMPLETED FOR L12
L13 4 DUP REM L12 (3 DUPLICATES REMOVED)

=> d 1-4 cbib abs

L13 ANSWER 1 OF 4 MEDLINE
1999199239 Document Number: 99199239. Factor-specific modulation of CREB-binding protein acetyltransferase activity. Perissi V; Dasen J S; Kurokawa R; Wang Z; Korzus E; Rose D W; Glass C K; Rosenfeld M G. (Howard Hughes Medical Institute, University of California at San Diego, La Jolla, CA 92093-0648, USA.)PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Mar 30) 96 (7) 3652-7. Journal code: PV3. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB CREB-binding proteins (CBP) and p300 are essential **transcriptional** coactivators for a large number of regulated **DNA**-binding **transcription** factors, including CREB, nuclear receptors, and STATs. CBP and p300 function in part by mediating the assembly of multiprotein complexes that contain additional cofactors such as p300/CBP interacting protein (p/CIP), a member of the p160/SRC family of coactivators, and the p300/CBP associated factor p/CAF. In addition to serving as molecular **scaffolds**, CBP and p300 each possess intrinsic acetyltransferase activities that are required for their function as coactivators. Here we report that the **adenovirus** E1A protein inhibits the acetyltransferase activity of CBP on binding to the C/H3 domain, whereas binding of CREB, or a CREB/E1A fusion protein to the KIX domain, fails to inhibit CBP acetyltransferase activity. Surprisingly, p/CIP can either inhibit or stimulate CBP acetyltransferase activity depending on the specific substrate evaluated and the functional domains present in the p/CIP protein. While the CBP interaction domain of p/CIP

inhibits acetylation of histones H3, H4, or high mobility group by CBP, it enhances acetylation of other substrates, such as Pit-1. These observations suggest that the acetyltransferase activities of CBP/p300 and p/CAF can be differentially modulated by factors binding to distinct regions of CBP/p300. Because these interactions are likely to result in differential effects on the coactivator functions of CBP/p300 for different classes of **transcription** factors, regulation of CBP/p300 acetyltransferase activity may represent a mechanism for integration of diverse signaling pathways.

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1999 ACS
1996:58252 Document No. 124:78726 **DNA** construct for effecting homologous recombination and uses for recombinant protein production. Treco, Douglas A.; Heartlein, Michael W.; Selden, Richard F. (Transkaryotic Therapies, Inc., USA). PCT Int. Appl. WO 9531560 A1 19951123, 147 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 95-US6045 19950511. PRIORITY:
US 94-243391 19940513.
AB The invention relates to constructs comprising: a) a **targeting sequence**; b) a regulatory sequence; c) an exon; and d) an unpaired splice-donor site. The invention further relates to a method of producing protein in vitro or in vivo comprising the homologous recombination of a construct as described above within the **cell**. The homologously recombinant **cell** is then maintained under conditions which will permit **transcription** and transition, resulting in protein expression. The present invention further relates to homologously recombinant **cells**, including primary, secondary, or immortalized vertebrate **cells**, methods of making the **cells**, methods of homologous recombination to produce fusion genes, methods of altering gene expression in the **cells**, and methods of making a protein in a **cell** employing the constructs of the invention.

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1999 ACS
1994:48303 Document No. 120:48303 Binding specificity of a nuclear **scaffold**: supercoiled, single-stranded, and **scaffold** -attached-region **DNA**. Kay, Volker; Bode, Juergen (Ges. Biotechnol. Forsch. m.b.H., Braunschweig-Stoeckheim, D-38124, Germany). Biochemistry, 33(1), 367-74 (English) 1994. CODEN: BICHAW. ISSN: 0006-2960.
AB **Scaffold**-attached-region (SAR) elements of **DNA** enhance **transcriptional** rates, and this has been correlated with their ability to undergo sepn. into single strands (ssDNA) under conditions of neg. superhelicity (Bode et al., 1992). The competition studies presented here suggest that the SAR-**scaffold** interaction is based, in part, on the recognition of single strands, while about one-half of SAR sites are inaccessible to ssDNA. Conversely, since there are 20,000 SAWR sites but more than 60,000 sites for ssDNA per nuclear equiv., not all ssDNA sites are open for SARs. In addn., a completely sep. set of binding centers recognizing and enzymically converting **DNA** of superhelical d. below -0.04 can be titrated. These findings reflect multiple binding specificities for **scaffold** prepns. that are

routinely used for screening **scaffold**-attached regions.

L13 ANSWER 4 OF 4 MEDLINE DUPLICATE 1
95112899 Document Number: 95112899. An actin infrastructure is associated with eukaryotic chromosomes: structural and functional significance.
Sauman I; Berry S J. (Wesleyan University, Biology Department, Middletown,
CT 06459-0170..)EUROPEAN JOURNAL OF CELL BIOLOGY, (1994 Aug) 64 (2) 348-56. Journal code: EM7. ISSN: 0171-9335. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.
AB The presence of actin in eukaryotic nuclei, and, especially, its functional significance has not been well established. We have found that under routine immunocytochemical conditions, no actin can be detected in insect follicle **cell** nuclei by means of antibody (both mono- and polyclonal) or phalloidin staining. However, a pretreatment of nuclear preparations with two different endonucleases (deoxyribonuclease I or micrococcal nuclease) to remove a substantial amount of chromosomal **DNA** uncovers the presence of nuclear actin for both antibody and phalloidin detection. Employing the same nuclease digestion followed by antibody or phalloidin staining with squash preparations of Drosophila polytene chromosomes revealed that the nuclear actin is directly associated with the chromosomes. A strong positive signal in the polytene chromosomes obtained with phalloidin labeling not only confirmed the presence of actin in the chromosomes, but indicates that a considerable amount of nuclear actin is present in filamentous form (F-actin) rather than monomeric (G-actin). The detection of actin associated with Xenopus embryo chromosomes suggests the significance of chromosomal actin for diploid vertebrate **cells**. Using the specific actin disrupting agent cytochalasin D, we have demonstrated the structural significance of nuclear actin in maintaining the **linear** integrity of polytene chromosomes. Further, we present evidence that **RNA** **polymerase** II closely interacts with the chromosomal actin **scaffold**, and that its association with chromosomes does not require the presence of **DNA**.

=> s nolan g?/au,in;s payan d?/au,in

'IN' IS NOT A VALID FIELD CODE
L14 89 FILE MEDLINE
L15 89 FILE CAPLUS
L16 147 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L17 82 FILE EMBASE
L18 10 FILE WPIDS

TOTAL FOR ALL FILES
L19 417 NOLAN G?/AU,IN

'IN' IS NOT A VALID FIELD CODE
L20 109 FILE MEDLINE
L21 99 FILE CAPLUS
L22 152 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L23 108 FILE EMBASE
L24 1 FILE WPIDS

TOTAL FOR ALL FILES
L25 469 PAYAN D?/AU,IN

=> s l19 and l25

L26 0 FILE MEDLINE
L27 1 FILE CAPLUS
L28 0 FILE BIOSIS
L29 0 FILE EMBASE
L30 1 FILE WPIDS

TOTAL FOR ALL FILES
L31 2 L19 AND L25

=> dup rem l31

PROCESSING COMPLETED FOR L31
L32 1 DUP REM L31 (1 DUPLICATE REMOVED)

=> d cbib abs

L32 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 1
1999:8108 Document No. 130:62960 Combinatorial enzymic complexes for drug screening. **Payan, Donald;** Nolan, Garry P. (Rigel Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 9856904 A1 19981217, 71 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 98-US11926 19980610. PRIORITY: US 97-873601 19970612.

AB The invention relates to the formation of novel in vivo combinatorial enzyme complexes for use in screening candidate drug agents for bioactivity. Thus, compns. of novel mixts. of enzymes in a spatially constricted or defined manner, i.e., by binding of the enzymes to a scaffold mol., are provided. This configuration of enzymes allows them to act on a precursor mol. in a novel or efficient manner to form a candidate bioactive agent which may then be screened for bioactivity. These scaffolds, and the corresponding enzymes, are introduced into a variety of different types of cells, generally using retroviral introduction of the nucleic acids encoding them. Precursor mols. are then added and the cells are screened for desired phenotypes.

=> s scaffold and (dna or rna) and (bind? or polymerase or transcript?) and (target? sequence or nls or golgi or mitochrondria?)

L33 3 FILE MEDLINE
L34 3 FILE CAPLUS
L35 2 FILE BIOSIS
L36 2 FILE EMBASE
L37 0 FILE WPIDS

TOTAL FOR ALL FILES
L38 10 SCAFFOLD AND (DNA OR RNA) AND (BIND? OR POLYMERASE OR TRANSCRIPT
?) AND (TARGET? SEQUENCE OR NLS OR GOLGI OR MITOCHRONDRIA?)

=> s l38 not (l32 or l12)

```
L39             0 S L32
L40             3 FILE MEDLINE
L41             1 S L32
L42             2 FILE CAPLUS
L43             0 S L32
L44             2 FILE BIOSIS
L45             0 S L32
L46             2 FILE EMBASE
L47             0 S L32
L48             0 FILE WPIDS

TOTAL FOR ALL FILES
L49             9 L38 NOT (L32 OR L12)

=> s l38 not (l31 or l12)

L50             3 FILE MEDLINE
L51             2 FILE CAPLUS
L52             2 FILE BIOSIS
L53             2 FILE EMBASE
L54             0 FILE WPIDS

TOTAL FOR ALL FILES
L55             9 L38 NOT (L31 OR L12)

=> dup reml 55

ENTER REMOVE, IDENTIFY, ONLY, OR (?):end


=> dup rem l55

PROCESSING COMPLETED FOR L55
L56              4 DUP REM L55 (5 DUPLICATES REMOVED)

=> d cbib abs 1-4


L56  ANSWER 1 OF 4  MEDLINE
1999138982  Document Number: 99138982.   Open reading frame 1a-encoded
subunits
     of the arterivirus replicase induce endoplasmic reticulum-derived
     double-membrane vesicles which carry the viral replication complex.
     Pedersen K W; van der Meer Y; Roos N; Snijder E J. (Division of Electron
     Microscopy, Department of Biology, University of Oslo, Oslo, Norway.
     )JOURNAL OF VIROLOGY, (1999 Mar) 73 (3) 2016-26.  Journal code: KCV.
ISSN:
     0022-538X. Pub. country: United States. Language: English.
AB   The replicase of equine arteritis virus (EAV; family Arteriviridae, order
     Nidovirales) is expressed in the form of two polyproteins (the open
     reading frame 1a [ORF1a] and ORF1ab proteins). Three viral proteases
     cleave these precursors into 12 nonstructural proteins, which direct both
     genome replication and subgenomic mRNA transcription.
     Immunofluorescence assays showed that most EAV replicase subunits
localize
     to membranes in the perinuclear region of the infected cell. Using
     replicase-specific antibodies and cryoimmunoelectron microscopy, unusual
     double-membrane vesicles (DMVs) were identified as the probable site of
     EAV RNA synthesis. These DMVs were previously observed in cells
     infected with different arteriviruses but were never implicated in viral
```

RNA synthesis. Extensive electron microscopic analysis showed that they appear to be derived from paired endoplasmic reticulum membranes and that they are most likely formed by protrusion and detachment of vesicular structures with a double membrane. Interestingly, very similar membrane rearrangements were observed upon expression of ORF1a-encoded replicase subunits nsp2 to nsp7 from an alphavirus-based expression vector. Apparently, the formation of a membrane-bound **scaffold** for the replication complex is a distinct step in the arterivirus life cycle, which is directed by the ORF1a protein and does not depend on other viral proteins and/or EAV-specific **RNA** synthesis.

L56 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 1
1998:768524 Document No. 130:148337 Molecular Basis for the **DNA** Sequence Selectivity of Ecteinascidin 736 and 743: Evidence for the Dominant Role of Direct Readout via Hydrogen Bonding. Seaman, Frederick C.; Hurley, Laurence H. (Drug Dynamics Institute College of Pharmacy, The University of Texas at Austin, Austin, TX, 78712, USA). J. Am. Chem. Soc., 120(50), 13028-13041 (English) 1998. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

AB The marine natural product ecteinascidin 743 (Et 743) is currently in phase II clin. trials. The authors have undertaken parallel structural and modeling studies of an Et 743-(N2-guanine) 12-mer **DNA** adduct and an adduct involving the structurally related Et 736 of the same sequence to ascertain the structural basis for the ecteinascidin-**DNA** sequence selectivity. In contrast to the C-subunit differences found in Et 736 and Et 743, they have identical A-B-subunit **scaffolds**, which are the principal sites of interaction with **DNA** bases. These identical **scaffolds** generate parallel networks of drug-**DNA** hydrogen bonds that assoc. the drugs with the three base pairs at the recognition site. The authors propose that these parallel hydrogen bonding networks stabilize the Et 736 and Et 743 A- and B-subunit prealkylation **binding** complex with the three base pairs and are the major factors governing sequence recognition and reactivity. The possibility that a unique hydrogen-bonding network directs the course of sequence recognition was examd. by first characterizing the hydrogen-bonding substituents using 1H NMR properties of the exchangeable protons attached to the hydrogen-bond donor and other protons near the proposed acceptor. Using these exptl. findings as indicators of hydrogen bonding, Et 736-12-mer duplex adduct models (**binding** and covalent forms) contg. the favored sequences 5'-AGC and 5'-CGG were examd. by mol. dynamics (MD) to evaluate the stability of the hydrogen bonds in the resulting conformations. The MD-generated models of these favored sequences display optimal donor/acceptor positions for maximizing the no. of drug-**DNA** hydrogen bonds prior to covalent reaction. The results of MD anal. of the carbinolamine (**binding**) forms of the sequences 5'-GGG (moderately reactive) and 5'-AGT (poorly reactive) suggested reasons for their diminished hydrogen-bonding capability. These exptl. and modeling results provide the structural basis for the following sequence specificity rules: For the **target sequence** 5'-XGY, the favored base to the 3'-side, Y, is either G or C. When Y is G, then a pyrimidine base (T or C) is favored for X. When Y is C, a purine (A or G) is favored for X.

L56 ANSWER 3 OF 4 MEDLINE
95352643 Document Number: 95352643. Nuclear multicatalytic proteinase alpha subunit RRC3: differential size, tyrosine phosphorylation, and susceptibility to antisense oligonucleotide treatment. Benedict C M; Ren L; Clawson G A. (Department of Pathology, Pennsylvania State University,

Hershey 17033, USA.)BIOCHEMISTRY, (1995 Jul 25) 34 (29) 9587-98. Journal
code: A0G. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB Multicatalytic proteinases (MCPs) are macromolecular structures involved in intracellular degradation of many types of proteins. MCPs are composed of a 20S "core" which consists of both structural (alpha) and presumed catalytic (beta) subunits in association with complexes of accessory proteins. Immunohistochemical studies have shown MCP subunits to be largely cytoplasmic, although nuclear localization is also observed. Reverse **transcription/polymerase** chain reaction amplifications were performed with redundant primers to conserved regions within known subunits, in an attempt both to identify potential new subunits and to define the repertoire of subunits expressed in hepatocytes. No new subunits were identified, and we found that RRC3, an alpha subunit of MCPs which contains a putative nuclear localization signal (**NLS**), was the predominant alpha subunit expressed in hepatocytes and hepatocyte-derived cell lines. Antibodies were developed against a unique C-terminal peptide region of RRC3. Immunohistochemical studies using affinity-purified antibodies showed that RRC3 has both cytoplasmic and nuclear localizations. Immunoprecipitation/immunoblot analyses showed that a significant proportion of nuclear RRC3 was associated with the nuclear **scaffold** (NS). NS RRC3 showed a significantly smaller M(r) (24,000) than the cytoplasmic form (M(r) 28,000), and only the nuclear form contained phosphotyrosine. In metabolic labeling experiments with [32P]orthophosphate, the major nuclear and NS form observed showed an M(r) of 24,000, whereas no labeling of cytosolic RRC3 was observed. A minor 32P-labeled band of M(r) 28,000 was also observed in nuclei, and this M(r) 28,000 form was found in the soluble nuclear extract within MCP complexes. These results suggest that tyrosine phosphorylation of the cytosolic form (M(r) 28,000) rapidly triggers nuclear import, which is in turn quickly followed by conversion to the major M(r) 24,000 form associated with NS. Treatment with antisense oligonucleotides targeted to the initiation site of RRC3 reduced the growth of a hepatocyte-derived cell line by 95% and produced a marked morphological change (in the absence of overt toxicity). Under these treatment conditions, RRC3 mRNA was dramatically reduced. RRC3 protein was also dramatically reduced in the NS, but showed only a small reduction in cytosol, suggesting that the nuclear RRC3 may be important in cell growth and differentiation.

L56 ANSWER 4 OF 4 MEDLINE DUPLICATE 2

94187728 Document Number: 94187728. Molecular genetic analyses of a 376-kilodalton **Golgi** complex membrane protein (giantin) [retracted in Mol Cell Biol 1995 Jan;15(1):591]. Seelig H P; Schranz P; Schroter H; Wiemann C; Griffiths G; Renz M. (Institute of Immunology and Molecular Genetics, Karlsruhe, Germany.)MOLECULAR AND CELLULAR BIOLOGY, (1994 Apr) 14 (4) 2564-76. Journal code: NGY. ISSN: 0270-7306. Pub. country: United States. Language: English.

AB Molecular genetic analyses of a 376-kDa **Golgi** complex (GC) membrane protein (giantin) are described. The immunoglobulin G fraction of a human serum containing antibodies against GC antigens as revealed by indirect immunofluorescence microscopy with Hep-2 cells was used to screen a HeLa cDNA expression library, yielding four overlapping cross-hybridizing clones. Additional cDNA clones were retrieved from a lambda gt11 human thyroid cDNA library or generated by reverse **transcriptase**-mediated PCR from HeLa cell mRNA. Alignment of the

clones resulted in a consensus cDNA of 10,300 bp encoding a protein of
376
kDa. The corresponding mRNA with a size of about 10 kb was detected by Northern (**RNA**) blotting of HeLa, Hep-G2, and Jurkat cell **RNA**. Sequence analyses of the protein revealed an extraordinarily high content of heptad repeats with the probability of forming coiled coils similar to the proteins of the myosin family. Five overlapping recombinant proteins covering the entire sequence were synthesized and used for antibody production in rabbits and for affinity purification of human and rabbit antibodies. Indirect immunofluorescence experiments also done with brefeldin A-treated Hep-2 and Pt K1 cells revealed an identical GC staining of both the affinity-purified human and rabbit antibodies. Double labeling experiments with antibodies against the GC marker mannosidase II as well as immunoelectron microscopic studies confirmed
the
localization of the protein within the GC. A corresponding endogenous large-molecular-mass protein of about 390 kDa was found in [35S]methionine-labeled Hep-2 cell lysates as well as in GC-enriched subcellular fractions from rat liver. The protein as well as the recently described proteins golgin-95 and golgin-160 (M. J. Fritzler, J. C. Hamel, R. L. Ochs, and E. K. L. Chan, J. Exp. Med. 178:49-62, 1993) may belong
to
a new group of **Golgi** proteins with a high content of heptad repeats which may exert functions in **scaffold** formation or vesicle transport. As far as can be concluded from immunological and personally communicated partial cDNA sequence data, the protein seems to be identical with a 400-kDa **Golgi** protein (giantin) recently described (A. D. Linstedt and H. P. Hauri, Mol. Biol. Cell 4:679-693, 1993). Therefore, we agreed to adopt the name giantin.

=> dis his

Insert the Sequence Listing as pages 58-68.

Renumber the Claims as pages 69-72.

Renumber the Abstract as page 73.

In the Claims:

1. (Amended) A cell containing a composition comprising:

a) an [exogeneous]exogenous scaffold having no enzymatic activity and comprising at least a first binding site and a second binding site; and

b) at least a first and a second enzyme, wherein at least one of said enzymes is heterologous to said cell;

wherein said first enzyme is bound to said first binding site and said second enzyme is bound to said second binding site.

2. (Amended) A cell containing a composition comprising:

a) nucleic acid encoding an [exogeneous]exogenous scaffold having no enzymatic activity and comprising at least a first binding site and a second binding site; and

b) nucleic acid encoding at least a first and a second enzyme, wherein at least one of said enzymes is heterologous to said cell;

wherein said first enzyme is capable of being bound to said first binding site and said second enzyme is capable of being bound to said second binding site.

3. A cell according to claim 1 or 2, wherein said scaffold comprises at least three binding sites.

4. A cell according to claim 1 or 2, wherein said scaffold comprises at least four binding sites.

5. A cell according to claim 1 or 2, wherein said scaffold comprises at least five binding sites.

6. A cell according to claim 1 or 2, wherein said binding sites are on the same scaffold molecule.

7. A cell according to claim 1 or 2, wherein said binding sites are on different scaffold molecules.

8. (Amended) A cell according to claim 1 or 2, further comprising

c) an [exogeneous]exogenous bioactive agent precursor.

9. ~~A method of screening~~ for a bioactive agent, said method comprising:

a) expressing in a plurality of host cells nucleic acid encoding an exogeneous scaffold comprising at least a first binding site and a second binding site;

b) expressing in said plurality of host cells nucleic acids encoding at least a first enzyme and a second enzyme; under conditions where said nucleic acids are expressed, and said first enzyme binds to said first binding site and said second enzyme binds to said second binding site;

c) screening said host cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a bioactive agent.

10. A method of screening for a bioactive agent, said method comprising:

a) expressing in a plurality of host cells a library of nucleic acids encoding a library of scaffolds, each scaffold comprising at least a first binding site and a second binding site;

b) expressing in said cells a library of nucleic acids encoding a library of enzymes; under conditions where said nucleic acids are expressed, and at least some of said enzymes bind to said scaffolds;

c) screening said host cells for an altered phenotype.

11. A method according to claim 9, wherein said expressing step further comprises introducing said nucleic acids into said cells.

12. A method according to claim 10, wherein said introduction comprises retroviral infection.

13. A method according to claim 9 further comprising adding at least one exogenous precursor to said cell.

Please add the following new claims:

--27. A cell according to claim 1 or 2, wherein said cell is a mammalian cell.

28. A cell according to claim 1 or 2, wherein said scaffold is linear.

29. A cell according to claim 1 or 2, wherein said scaffold is circular.

30. A cell according to claim 1 or 2, wherein said scaffold is branched.

31. A cell according to claim 1 or 2, wherein said scaffold further comprises a fusion partner.

32. A cell according to claim 1 or 2, wherein at least one of said enzymes further comprises a fusion partner.

33. A cell according to claim 31, wherein said fusion partner is a presentation structure.

34. A cell according to claim 31, wherein said fusion partner is a targeting sequence.

35. A cell according to claim 31, wherein said fusion partner is a rescue sequence.

36. A cell according to claim 31, wherein said fusion partner is a stability sequence.

37. A cell according to claim 31, wherein said fusion partner is a linker sequence.

38. A cell according to claim 32, wherein said fusion partner is a presentation structure.

39. A cell according to claim 32, wherein said fusion partner is a targeting sequence.

40. A cell according to claim 32 wherein said fusion partner is a rescue sequence.

41. A cell according to claim 32, wherein said fusion partner is a stability sequence.

42. A cell according to claim 32, wherein said fusion partner is a linker sequence.--